

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY


(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 18 JUL 2005

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Applicant's or agent's file reference 101064-1 WO		FOR FURTHER ACTION See Form PCT/PEA/416	
International application No. PCT/GB2004/003473	International filing date (day/month/year) 12.08.2004	Priority date (day/month/year) 15.08.2003	
International Patent Classification (IPC) or national classification and IPC C07D333/38, C07D409/12, A61K31/38, A61P35/00			
Applicant ASTRAZENECA AB			
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>			
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>			
Date of submission of the demand 02.06.2005		Date of completion of this report 15.07.2005	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer Bakboord, J Telephone No. +49 89 2399-	



**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/GB2004/003473

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

Description, Pages

1-79 as originally filed

Claims, Numbers

1-28 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/GB2004/003473

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 20-25

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 20-25

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

**INTERNATIONAL PRELIMINARY REPORT
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International application No.
PCT/GB2004/003473

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	2-5, 7, 9, 11-17
	No: Claims	1, 6, 8, 10, 18-27, 28
Inventive step (IS)	Yes: Claims	1-17
	No: Claims	1-28
Industrial applicability (IA)	Yes: Claims	1-19, 26-28
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 20-25 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

V.1 The present application relates to 2-ureido-3-amido-5-phenyl substituted thiophenes and their use as checkpoint kinase 1 inhibitors.

V.2 Reference is made to the following documents:

D1: WO 03/029241 A

D2: WO 03/028731 A

D3: WO 02/070494 A

V.3 Novelty

Document D1 discloses a compound of formula I in which R¹ is hydrogen, R² is methyl, R⁴ is methyl and R⁵ is methyl (example 28). Moreover document D1 discloses 2-ureido-3-amido-5-phenyl substituted thiophenes and their use as checkpoint kinase 1 inhibitors (claim 5).

Document D1 also discloses the use of a compound of formula VI in the manufacture of a compound of formula I (scheme II).

Document D2 discloses 2-amido-3-ureido-5-phenyl substituted thiophenes and their use as checkpoint kinase 1 inhibitors (claim 6).

Document D3 discloses phenyl rings substituted with groups C(O)NR¹R², N(H)C(O)N(H)R⁴ and OR⁵ (see e.g. compounds 1-6) to be used as checkpoint kinase 1 inhibitors.

A compound of formula I for the use as checkpoint inhibitors is disclosed in document D1. Claims 1, 6, 8, 10, 18-27 therefore do not fulfill the requirements of

Article 33(2) PCT.

A compound of formula I as described in claims 2-5, 7, 9, 11-17 is disclosed in none of the documents. These claims therefore fulfill the requirements of Art 33(2) PCT.

The use of a compound of formula VI for the manufacture of a compound of formula I is disclosed in document D1. Claim 28 therefore does not fulfill the requirements of Art 33(2) PCT.

V.4 Inventive step

As the use of thiophene 2-ureido-3-amido-5-phenyl substituted thiophenes for the inhibition of checkpoint kinase 1 is known from document D1 the present application cannot be considered to involve an inventive step (Art 33(3) PCT).

V.5 Industrial applicability

For the assessment of the present claims 20-25 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.